



Contents lists available at ScienceDirect

Chinese Journal of Traumatology

journal homepage: <http://www.elsevier.com/locate/CJTEE>

Original Article

Should we change our approach to resuscitating victims of femoral fracture? A clinical experience in a busy trauma hospital in Shiraz, Iran

Shahram Paydar, Ali Taheri Akerdi, Sadra Nikseresht, Hossein Abdollahzadeh-Fard, Leila Shayan, Zahra Ghahramani*, Shahram Bolandparvaz, Hamid Reza Abbasi

Trauma Research Center, Rajaei (Emtiaz) Trauma Hospital, Shiraz University of Medical Sciences, Shiraz, Iran

ARTICLE INFO

Article history:

Received 18 April 2020

Received in revised form

1 June 2020

Accepted 6 June 2020

Available online 15 August 2020

Keywords:

Resuscitation

Victims

Femoral fractures

Hemorrhagic shock

ABSTRACT

Purpose: Traumatic hemorrhagic shock is a life-threatening event worldwide. Severe brain trauma accompanying femoral fractures can trigger inflammatory responses in the body and increase pre-inflammatory cytokines such as TNF- α , IL-1. The primary treatment in these cases is hydration with crystalloids, which has both benefits and complications. The purpose of this study was to investigate the effects of fluid therapy on the hemodynamics, coagulation profiles, and blood gases in such patients.

Methods: In this cross-sectional study, patients were divided into two groups: femoral fracture group and non-femoral group. The hemodynamic status, coagulation profile, and blood gases of patients in both groups were evaluated upon arrival at the hospital and again 2 h later. Data were analyzed by *t*-test and ANOVA with repeated data and paired samples *t*-test.

Results: A total of 681 trauma patients (605 men and 76 women) participated in this study, including 69 (86.3%) men and 11 (13.8%) women in femoral fracture group and 536 men (89.2%) and 65 women (10.8%) in non-femoral group. The laboratory parameters were evaluated in response to the equal amount of crystalloid fluid given upon arrival and 2 h later. Blood gases decreased in the fracture group despite fluid therapy ($p < 0.003$), and the coagulation profile worsened although the change was not statistically significant.

Conclusion: The treatment of multiple-trauma patients with femoral bone fractures should be more concerned with the need for the infusion of vasopressors such as norepinephrine. If there is evidence of clinical shock, excessive crystalloid infusion (limited to 1 L) should be avoided, and blood and blood products should be started as soon as possible.

© 2020 Chinese Medical Association. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Shock is defined as “inadequate organ perfusion mode”; hence, fluid therapy is an important component in the rehabilitation of trauma patients along with the establishment of an airway and respiration.^{1–3} Initial hydration in cases of hypovolemic shock should expand intravascular volume, improve arterial mean pressure, improve heart function, provide perfusion, and reduce acidosis, hypothermia, and coagulopathy.⁴

Trauma and hypoperfusion cause various compensatory mechanisms to start in the body, through which catecholamines such as epinephrine, norepinephrine, and dopamine are released. Pain

causes a similar response, increases heart rate, and causes tachycardia. With these mechanisms, vasoconstriction occurs and blood is shifted to the vital organs.¹ Reduced blood flow to the organs also causes ischemia, anaerobic metabolism, and increased lactate production.^{1,2} Studies have shown that various injuries such as femoral fractures in brain-injured victims and shock can trigger inflammatory responses in the body and increase pre-inflammatory cytokines such as TNF- α , IL-1 and IL-6.^{2,5,6} Eventually systemic inflammatory response syndrome (SIRS) occurs.^{2,5,7,8} Shock is categorized in four main groups: hypovolemic, cardiogenic, distributive, and obstructive types. Many trauma patients can be classified into these main groups, but some patients exhibit another form of shock now known as traumatic shock. Acute respiratory distress syndrome (ARDS), coagulopathy, and multiple organ dysfunction syndrome (MODS) can be consequences of severe shock, delayed treatment of shock, or badly managed shock.²

* Corresponding author.

E-mail address: ghahreman2@yahoo.co.nz (Z. Ghahramani).

Peer review under responsibility of Chinese Medical Association.

In trauma, the basis of treatment for hypovolemia is initially fluid therapy with an infusion of 1–2 L of isotonic serum, despite having knowledge of complications such as progressive coagulopathy or reduced oxygen delivery capacity.^{1–9} However, the severity of the damage and the inflammatory process as well as the response of the body to the fluid in the treatment of various traumas are different.¹ The present study investigated the effects of infusion of one to two liters of crystalloids according to the ninth edition of the Advanced Trauma Life Support (ATLS) in trauma patients with and without femoral bone fracture.

Methods

After obtaining approval from the Ethics Committee of the Shiraz University of Medical Sciences, patient's records data were retrospectively studied from the Shahid Rajaee Hospital database, Shiraz Trauma Center on trauma patients aged 16–60 years with multiple traumas from years 2016 and 2017. Patients were divided into two groups: those with and those without femoral bone fractures along with other traumas. Patients transferred from other centers, those with known liver disease, and those with anti-platelet and anticoagulant drug consumption were excluded from the study.

Demographic data, vital signs, blood gas analyses, and coagulation profiles of patients were collected. Patients in both groups were matched in terms of multiple injuries, including brain, chest, or abdominal damage and pelvic fractures; the only difference between them was in terms of having or not having a femoral bone fracture. Injury Severity Score (ISS) was used to measure these patients in both groups. ISS has been one of the scoring modalities and we divided both femoral and non-femoral fractures based on the similarity of ISS.

Immediately upon the patient's arrival at the hospital and before any action was taken, the age, gender, vital signs (blood pressure, pulse rate and respiratory rate), and Glasgow coma scale of each patient were recorded. Then, blood samples were taken from patients for blood gas analyses (pH, HCO₃ and base deficit (BD)) and coagulation profiles as prothrombin time (PT), partial thromboplastin time (PTT), international normalized ratio (INR), and fibrinogen level.

Table 1

Comparison of the patients in two groups in terms of sex, age, amount of fluid intake and level of consciousness.

Group	Gender		Age (years)	GCS score	Fluid intake (mL)
	Male	Female			
Femoral fracture	69 (86.3)	11 (13.8)	33 ± 14	12.9 ± 3.3	1586 ± 1174
Non-femoral fracture	536 (89.2)	65 (10.8)	31.4 ± 13	12.5 ± 3.5	1476 ± 909
<i>p</i> value	0.688		0.343	0.392	0.342

Data are expressed as mean ± standard deviation except for "Gender", which are expressed as *n* (%). GCS: Glasgow coma scale.

Table 2

Vital signs before and 2 h after fluid therapy in two groups, mean ± standard deviation.

Group	SBP (mmHg)	RR (breaths/min)	HR (beats/min)
Femoral fracture			
At arrival	120 ± 20	19.5 ± 5.9	107 ± 21
At 2 h	101 ± 49	15.4 ± 7.3	97 ± 34
<i>p</i> value within group	0.003	<0.001	0.008
Non-femoral fracture			
At arrival	124 ± 20	19 ± 3.6	98 ± 20
At 2 h	125 ± 19	18.1 ± 4.5	93 ± 18
<i>p</i> value within group	0.828	0.015	<0.001
<i>p</i> value between two groups	<0.001	0.001	0.001

SBP: systolic blood pressure; RR: respiratory rate; HR: heart rate.

According to the ATLS protocol,¹⁰ patients were hydrated with 1–2 L of crystalloids, and these variables were measured again one and 2 h later to evaluate the effects of the crystalloid infusion on these variables.

Statistical analysis

Statistical analysis was performed using SPSS 20 software. Data were analyzed by *t*-test and ANOVA with repeated data and paired-samples *t*-test. A *p* value level less than 0.05 was considered significant.

Results

After meeting the criteria for participation in the study, 681 trauma patients (605 men and 76 women) were included. Among them, 80 had femoral fracture, including 69 (86.3%) men and 11 (13.8%) women, and 601 did not have femoral fracture, presented as 536 men (89%) and 65 women (10.8%). The mean age of the patients was 31.6 years (Table 1).

Vital signs

After the initial treatment of fluids, the average blood pressure in the first 2 h decreased in the femoral fracture group (120.1–101.7 mmHg) and increased in the non-femoral fracture group (124.9–125.2 mmHg). The difference in mean blood pressure between the two groups after the initial treatment was significant (*p* < 0.001). In both groups, fluid therapy reduced the means of respiratory and heart rates in the first 2 h (Table 2).

Blood gas

The femoral fracture group had lower pH values in arterial blood gas before and after hydration than the non-fracture group. According to Table 3, the mean pH level and bicarbonate concentration were lower and the base deficit was greater in the fracture group than in the non-fracture group. It seems that hydration with more than 1 L worsened the blood gas variables after 2 h in all traumatized patients.

Table 3
Blood gas value before and 2 h after fluid resuscitation in two groups.

Group	pH	HCO ₃ (mmol/L)	BE (mmol/L)
Femoral fracture			
Before resuscitation	7.33 ± 0.11	21.3 ± 4.8	-3.6 ± 5.1
After resuscitation	7.31 ± 0.14	19.3 ± 3.5	-5.2 ± 4.8
p value	0.115	0.004	0.006
Non-femoral fracture			
Before resuscitation	7.35 ± 0.09	23.1 ± 4.2	-1.4 ± 4.3
After resuscitation	7.34 ± 0.09	20.7 ± 4.1	-3.4 ± 4.6
p value	0.002	<0.001	<0.001

BE: base excess.

Hemoglobin and coagulation profile

The mean of hemoglobin decreased in both groups after hydration; the decline was more evident in the femoral fracture group ($p < 0.001$). The range in the femoral fracture group was 12.4–10.5 g/L and in the non-femoral fracture group was 13.8–12.2 g/L. Hydration also worsened the factors in the coagulation profile, with significant changes only in the PTT values of both groups. There was no significant difference in PT and INR values before and after hydration. It should be noted, however, that the fracture group had higher PT, PTT, and INR levels.

A significant reduction was seen in the mean value of fibrinogen after hydration in both groups, particularly in the non-femoral fracture group. Table 4 shows the values for hemoglobin and coagulation profiles.

Discussion

Fluid therapy is an important component of the management of trauma patients. Fluid therapy to patients was based on ATLS guideline (10th edition).¹⁰

The present study aimed to investigate the effects of fluid therapy on the vital signs, blood gas analyses, and coagulation profiles of patients with or without femoral bone fractures.

The results showed that patients with bone fracture experienced a decrease in heart and respiratory rates after crystalloid infusion. Moreover, these patients had more acidosis and greater disruption of their coagulation profiles. According to other studies, patients with long bone fractures secrete higher levels of mediators and inflammatory cytokines such as TNF- α , IL-1 and IL-6, which pushes the body into the inflammatory phase.^{2,5,6} Today, these changes are attributed to traumatic shock, which can lead to the onset of SIRS and other unpleasant consequences, including ARDS, coagulopathy, and MODS.^{2,5,7,8}

As with septic shock, traumatic shock leads to vasodilation and increases the permeability of the vessels; as a result, the fluid will outflow into the extravascular space.² In these situations, crystalloid fluid therapy is controversial; some support restricting fluid

and diuretic therapy, and some agree with liberal fluid therapy.² Based on the results of the current study, unlike in patients without femoral fractures, patients with bone fractures experienced a drop in blood pressure, despite fluid therapy. Thus, the question of whether action other than fluid therapy is necessary in these patients is raised.

The European Guideline for Bleeding and Coagulopathy Management¹¹ recommends the use of a vasopressor, such as norepinephrine, in conjunction with fluid therapy to maintain arterial pressure and tissue perfusion. It is also believed that norepinephrine causes visceral blood flow to vital organs.¹¹ Despite the controversy over vasopressor injection in trauma patients,¹² some studies have confirmed its use^{13,14} and have shown that it can improve cardiac output and increase inferior vena cava (IVC) flow.¹³

Another action may be the reduction of crystalloid infusion and the early use of blood products in these patients. Although the complications of blood transfusion in conditions other than trauma are considered to be between 7 and 9,^{11–15} these values are acceptable in the acute phase of trauma.^{16,17} Under such circumstances, the use of heart rate, blood pressure (also shock index), and base deficit in making decisions about blood transfusions seems more rational.^{1,18} Therefore, in the acute phase of trauma, a number of 7–9 is not very suitable. If there is a clinical presentation of shock in the patient based on the heart rate, blood pressure, and base deficit values after one to two liters of crystalloids, blood and blood products should be given, as more crystalloid infusion reduces oxygen carrying capacity and increases coagulopathy.³

Using colloid resuscitation in femoral fracture group and severe trauma patients has a worsening prognosis. A study¹⁹ investigated the safety and efficacy of synthetic colloid resuscitation among severely trauma patients. This study suggests that synthetic colloid resuscitation provide no beneficial effects and will be harmful in patients who are severe trauma. The results of this study also support international and national guideline, which recommend using crystalloid in trauma patients.

Another study determined the effect of resuscitation deaths on colloid fluids compared with crystalloid resuscitation. Revitalization with colloids was associated with an increased risk of 4% mortality. This systematic review did not support using colloids to replace volume in critically ill patients.²⁰

Based on the results of the present study, it is recommended that the treatment of multiple-trauma patients with femoral bone fractures be more concerned with the need for the infusion of vasopressors such as norepinephrine; if there is evidence of clinical shock, excessive crystalloid infusion (limited to 1 L) should be avoided, and the infusion of blood and blood products should be initiated as soon as possible. The amount of crystalloid between the two groups did not differ statistically. Giving 1 L of crystalloid is the minimum amount based on ATLS protocol. Some patients will receive 2 L because we do not have blood refrigerator room and

Table 4
Coagulation and hemoglobin level before and after fluid resuscitation in two groups.

Group	Hb (g/L)	PTT (s)	PT (s)	INR	Fibrinogen (g/L)
Femoral fracture					
Before resuscitation	12.4 ± 2.2	33.3 ± 8.9	13.8 ± 2.8	1.3 ± 0.5	229.3 ± 117.1
After resuscitation	10.5 ± 2.5	36.7 ± 11.6	14.5 ± 3.4	1.9 ± 0.4	82.3 ± 133.2
p value	<0.001	0.038	0.210	0.247	<0.001
Non-femoral fracture					
Before resuscitation	13.8 ± 3.6	33.2 ± 6	13.2 ± 1.8	1.1 ± 0.3	233.3 ± 93.6
After resuscitation	12.2 ± 2.1	35.4 ± 9.3	13.2 ± 2.2	1.2 ± 0.2	59.5 ± 11.3
p value	<0.001	<0.001	0.864	0.436	<0.001

Hb: hemoglobin, PTT: partial thromboplastin time, PT: prothrombin time, INR: international normalized ratio.

sometimes it is necessary to give another 1 L of crystalloid to receive blood from the blood bank.

Funding

There has been no significant financial support for this work that could have influenced its outcome.

Ethical statement

This study was approved by the Ethics Committee of the Shiraz University of Medical Sciences.

Declaration of competing interest

We wish to confirm that there are no known conflicts of interest associated with this publication.

References

- Cottingham CA. Resuscitation of traumatic shock: a hemodynamic review. *AACN Adv Crit Care*. 2006;17:317–326. <https://doi.org/10.1097/01256961-200607000-00011>.
- Anderson MW, Watson GA. Traumatic shock: the fifth shock. *J Trauma Nurs*. 2013;20:37–43. <https://doi.org/10.1097/JTN.0b013e318286620a>.
- Sisak K, Dewar D, Butcher N, et al. The treatment of traumatic shock: recent advances and unresolved questions. *Eur J Trauma Emerg Surg*. 2011;37:567–575. <https://doi.org/10.1007/s00068-011-0150-1>.
- Han J, Ren HQ, Zhao QB, et al. Comparison of 3% and 7.5% hypertonic saline in resuscitation after traumatic hypovolemic shock. *Shock*. 2015;43:244–249. <https://doi.org/10.1097/SHK.0000000000000303>.
- Kobbe P, Vodovotz Y, Kaczorowski DJ, et al. Patterns of cytokine release and evolution of remote organ dysfunction after bilateral femur fracture. *Shock*. 2008;30:43–47. <https://doi.org/10.1097/SHK.0b013e31815d190b>.
- Probst C, Mirzayan MJ, Mommsen P, et al. Systemic inflammatory effects of traumatic brain injury, femur fracture, and shock: an experimental murine polytrauma model. *Mediators Inflamm*. 2012;2012. <https://doi.org/10.1155/2012/136020>, 136020.
- Levy RM, Prince JM, Yang R, et al. Systemic inflammation and remote organ damage following bilateral femur fracture requires Toll-like receptor 4. *Am J Physiol Regul Integr Comp Physiol*. 2006;291:R970–R976. <https://doi.org/10.1152/ajpregu.00793.2005>.
- Kobbe P, Vodovotz Y, Kaczorowski DJ, et al. The role of fracture-associated soft tissue injury in the induction of systemic inflammation and remote organ dysfunction after bilateral femur fracture. *J Orthop Trauma*. 2008;22:385–390. <https://doi.org/10.1097/BOT.0b013e318175dd88>.
- Martini WZ, Dubick MA, Blackburne LH. Comparisons of lactated Ringer's and Hextend resuscitation on hemodynamics and coagulation following femur injury and severe hemorrhage in pigs. *J Trauma Acute Care Surg*. 2013;74:732–739. <https://doi.org/10.1097/TA.0b013e31827f156d>.
- 10th Edition of the Advanced Trauma Life Support® (ATLS®) Student Course Manual. Chicago (IL): American College of Surgeons; 2018.
- Rossaint R, Bouillon B, Cerny V, et al. The European guideline on management of major bleeding and coagulopathy following trauma. *Crit Care*. 2016;20:100. <https://doi.org/10.1186/s13054-016-1265-x>, fourth ed.
- Rochweg B, Hylands M, Møller M, et al. CCCS-SSAI WikiRecs clinical practice guideline: vasopressors in early traumatic shock. *Can J Anaesth*. 2017;64:766–768. <https://doi.org/10.1007/s12630-017-0879-z>.
- Giraud R, Siegenthaler N, Arroyo D, et al. Impact of epinephrine and norepinephrine on two dynamic indices in a porcine hemorrhagic shock model. *J Trauma Acute Care Surg*. 2014;77:564–569. <https://doi.org/10.1097/TA.0000000000000409>.
- Fangio P, Asehnoune K, Edouard A, et al. Early embolization and vasopressor administration for management of life-threatening hemorrhage from pelvic fracture. *J Trauma*. 2005;58:978–984. <https://doi.org/10.1097/01.TA.0000163435.39881.26>.
- Polytrauma Guideline Update Group. Level 3 guideline on the treatment of patients with severe/multiple injuries: AWMF Register-Nr. 012/019. *Eur J Trauma Emerg Surg*. 2018;44:3–271. <https://doi.org/10.1007/s00068-018-0922-y>.
- Figueiredo S, Taconet C, Harrois A, et al. How useful are hemoglobin concentration and its variations to predict significant hemorrhage in the early phase of trauma? A multicentric cohort study. *Ann Intensive Care*. 2018;8:76. <https://doi.org/10.1186/s13613-018-0420-8>.
- Shahi V, Shahi V, Mower WR. Using serial hemoglobin levels to detect occult blood loss in the early evaluation of blunt trauma patients. *J Emerg Med*. 2018;55:307–312. <https://doi.org/10.1016/j.jemermed.2018.06.017>.
- El-Menyar A, Goyal P, Tilley E, et al. The clinical utility of shock index to predict the need for blood transfusion and outcomes in trauma. *J Surg Res*. 2018;227:52–59. <https://doi.org/10.1016/j.jss.2018.02.013>.
- Hilbert-Carius P, Schwarzkopf D, Reinhart K, et al. Synthetic colloid resuscitation in severely injured patients: analysis of a nationwide trauma registry (Trauma Register DGU). *Sci Rep*. 2018;8:11567. <https://doi.org/10.1038/s41598-018-30053-0>.
- Lu YQ, Cai XJ, Gu LH, et al. Experimental study of controlled fluid resuscitation in the treatment of severe and uncontrolled hemorrhagic shock. *J Trauma Acute Care Surg*. 2007;63:798–804. <https://doi.org/10.1097/TA.0b013e31815202c9>.